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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,438	03/21/2007	Ajay Verma	044508-5008-US	6971

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EXAMINER	
LOVE, TREVOR M	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
11/03/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,438	VERMA ET AL.	
	Examiner	Art Unit	
	TREVOR M. LOVE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,11,13-15 and 18-38* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,13-15 and 24-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/07/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/07/2010 has been entered.

Claims 1-5, 11, 13-15, and 18-38 are pending.

Claims 1-5 and 18-23 are withdrawn.

Claims 11 and 13 are currently amended.

Claims 11, 13-15, and 24-38 are currently under consideration.

Withdrawn Rejections

The rejection of claims 11, 13-15, and 24-38 under 35 U.S.C. 103(a) as being unpatentable over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Aminova et al (Pro-survival and pro-death effects of HIF-1α stabilization in a murine hippocampal cell line) and Lu et al (Hypoxia-inducible factor 1 Activation by Aerobic Glycolysis Implicates the Warburg Effect in Carcinogenesis) is withdrawn in view of Applicant's amendment to claim 13, and in view of the lack of clarity as to the role of the Aminova et al reference.

It is noted that a new grounds of rejection over the same references is newly presented below in better format as to provide a clear record.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11, 14, 15, 24-27, 29, 30, and 34 rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al (U.S. Patent number 5,602,183, Patent issued Feb. 11, 1997) as evidenced by the specification.

Martin teaches a wound healing composition comprising pyruvate (see entire document, for instance, Abstract and column 20, lines 55-67). Martin further teaches that the composition is used for wound healings such as lacerations or burns. Said composition can be used orally, topically, ophthalmically, or anorectally (see entire document, for instance column 21, first paragraph). Said composition is further in the form of sprays, creams, lozenges, tablets, foams, and suppositories (see entire document, for instance, column 23, lines 36-52 and column 21, first paragraph).

As evidenced by the specification "the endogenous 2-oxoacids pyruvate and oxaloacetate compete for the 2-oxoglutarate binding site in HIF hydroxylating enzymes and then lead to their inactivation. This results in long-lasting HIF-1α accumulation and activation of HIF-1α mediated gene expression, even in the presence of oxygen" (see instant specification, page 14, first paragraph). Therefore, that the method of Martin, which teaches the administration of, for example, pyruvate, would necessarily induce HIF-1 mediated gene expression. Merely discovering and claiming a new benefit of an *old* process cannot render the process again

patentable. *Verdegaal Bros., Inc. v. Union Oil Co. of Calif.,* 814 F.2d 628, 632-33, 2USPQ2d 1051, 1054 (Fed. Cir.), cert. Denied, 484 U.S. 827 (1987). *In re Woodruff*, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990), which states "a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." Further, the preamble and the intended use of the composition are necessarily met by the method of Martin. Specifically, administration of an identical active (such as pyruvate), to the same patient population (those with wounds and hence, in need of neovascularization), in the amount required by the claims (an amount) would necessarily result in neovascularization.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11, 14, 15, 24-31, and 33-38 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification. Note citations based on the PreGrant Publication. Further, support dates for limitations directed to human subjects, delivery of oxaloacetate and pyruvate, patient having surgery and intravenous administration include 08/01/2002, 12/04/2002, and

07/31/2003. Support dates for limitations directed to the activesalpha-keto-isovalerate, alpha-keto-isocaproate, and alpha-keto-beta-methylvalerate, and the administration routes of rectal, nasal, buccal, ocular, oral, and the composition is in the form of emulsions, sprays, enemas, ocular injections, or tablets include 12/04/2002 and 07/31/2003. Support dates for the topical application of the active include 07/31/2003.

Teichberg teaches a method of reducing extracellular brain glutamate levels by delivering a therapeutic amount of an active (see Abstract). Said composition comprises an active agent that is taught as being selected from oxaloacetate diethylester, oxaloacetate, pyruvate, α-ketoisocaproate, α-ketoisovalerate, α-keto-β-methylvalerate (see entire document, for instance [0025]), this reads on **instant claims 11 and 34-38**. Teichberg teaches that the preferred subjects of said method are canines, felines, ovines, porcines, equines, bovines, and humans (see entire document, for instance [0102]), this reads on the limitation of "human subject" in **instant claim 11**. Said method is also taught as being useful for reducing brain glutamate levels in patients having coronary artery bypass surgery and open heart surgery, which is a treatment for severe atherosclerosis. Furthermore, a patient having said surgery would necessarily be in need of wound healing (see claim 61), this reads on **instant claim 14**. Teichberg teaches that the composition can be applied topically (see entire document, for instance [0126] and [0134]), this reads on **instant claim 15**. Teichberg also teaches that the composition can be administered rectally via enemas (see entire document, for instance [0146]), by the nasal route via a spray (see entire document, for instance [0142]), orally via a capsule (see entire document, for instance [0140]), ocularly via intraocular injection, which would encompass solutions and suspensions (see entire document, for instance [0133] and [0144]), and subcutaneously via an injection of a

pharmaceutical composition which comprises a carrier (see entire document, for instance [0133] and 0127]), these read on **instant claims 24-26, and 27, 28, 29, 30, and 31, respectively**. Teichberg identifies that the composition comprises lipophilic solvents or vehicles such as fatty oils when the composition is being administered parenterally (see entire document, for instance [0144]). Teichberg identifies that in certain scenarios, for instance, in brain surgery, the composition is applied topically (see [0126]). Teichberg also teaches that the composition can be administered in a plurality of administrations over several days or weeks and that a skilled artisan would be able to vary the amount in order to meet the specific needs of the scenario (see [0152] and [0153]), this reads on **instant claim 33**.

As evidenced by the specification "the endogenous 2-oxoacids pyruvate and oxaloacetate compete for the 2-oxoglutarate binding site in HIF hydroxylating enzymes and then lead to their inactivation. This results in long-lasting HIF-1α accumulation and activation of HIF-1α mediated gene expression, even in the presence of oxygen" (see instant specification, page 14, first paragraph). Therefore, the method of Teichberg, which teaches the administration of, for example, pyruvate, would necessarily induce HIF-1 mediated gene expression. Merely discovering and claiming a new benefit of an *old* process cannot render the process again patentable. *Verdegaal Bros., Inc. v. Union Oil Co. of Calif.,* 814 F.2d 628, 632-33, 2USPQ2d 1051, 1054 (Fed. Cir.), cert. Denied, 484 U.S. 827 (1987). *In re Woodruff*, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990), which states "a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." Further, the preamble and the intended use of the composition are necessarily met by the composition of Teichberg. Specifically, administration of an identical active (such as pyruvate), to the same patient

population (those with wounds and hence, in need of neovascularization), in the amount required by the claims (an amount) would necessarily result in neovascularization.

One of ordinary skill in the art would utilize any one of oxaloacetate, pyruvate, α-ketoisocaproate, α-ketoisovalerate, α-keto-β-methylvalerate as the active in the composition of Teichberg. One would have been motivated to do so since Teichberg teaches said actives in a short list of preferred active ingredients in paragraph [0025]. There would be a reasonable expectation of success in the use of said active since they are directly taught by Teichberg.

With regard to the method of utilizing the composition being directed to promoting tissue neovascularization, it has been established that the composition is taught by Teichberg to be utilized on patients who are having coronary artery bypass surgery, which, like any major surgery, would require wound healing and neovascularization. Teichberg is teaching that the actives utilized in Teichberg reduce the amount of glutamate, which is useful for patients that are having surgery. Thus, the patient population in Teichberg whose glutamate levels are decreased would necessarily show increased HIF-1 expression. This is evidenced by the instant specification (for instance, page 14, first paragraph), and Semenza evidencing that accumulation of HIF results in neovascularization (see Semenza, entire document, for instance, Abstract). Hence, since the administration of the composition of Teichberg would necessarily induce HIF-1 mediated gene expression, there would also necessarily be neovascularization occurring in the patient with whom the composition of Teichberg is being administered.

Response to Arguments

Applicant argues in the response filed 07/07/2010 that the Aminova reference does not qualify as prior art, and that the Office's reliance upon Aminova is improper. Applicant's

argument is not found persuasive. It is noted that said reference is no longer relied upon. Furthermore, Applicant's argument that the teachings of Teichberg are entirely irrelevant is not found persuasive, particularly in view of the new grounds of rejection set forth above. Applicant further argues that Teichberg teaches a laundry list of agents that are effective in reducing extracellular brain glutamate levels. Applicant's argument is not found persuasive since the list in paragraph [0025] of Teichberg includes only 22 specific compounds. It would be within the skill of one of ordinary skill in the art to select any one of said clearly named actives. Teichberg clearly teaches the same components, the same methods of delivery, and the same patient population, therefore, the reliance upon Teichberg is proper. It is noted that MPEP 2112 states: "Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)." It is further noted that the art is not required to teach the same reasoning for adding components as Applicant, MPEP 2144 (IV) states "the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by Applicant. See, e.g., In re Kahn, 411 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)."

Claims 11, 13-15, 24-31, and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification as applied to claims 11,

14, 15, 24-31, and 33-38 above, and further in view of Fujii et al (2002, European Journal of Cardio-Thoracic Surgery).

The teachings of Teichberg, Semenza, and the instant specification are set forth above.

Teichberg fails to directly identify that the patient is suffering from thrombosis.

Fujii teaches that open heart surgery is a known useful treatment for posttraumatic inferior vena caval thrombosis (see entire document, for instance, Title).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the method of Teichberg in a patient who is suffering from thrombosis since the method of Teichberg is taught as being useful for patients having open heart surgery, and Fujii teaches that open heart surgery is a known useful treatment for thrombosis. There would be a reasonable expectation of success since Teichberg is generically drawn to all patients having open heart surgery, and Fujii exemplifies that a known population of those having open heart surgery are having said surgery due to thrombosis.

Claims 11, 14, 15 and 24-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification as applied to claims 11, 14, 15, 24-31, and 33-38 above, and further in view of Dykstra (U.S. PreGrant Publication number 2003/0212134).

The teachings of Teichberg, Semenza, and the instant specification are set forth above, wherein it is again noted that Teichberg identifies that the composition comprises lipophilic solvents or vehicles such as fatty oils (see entire document, for instance [0144]).

Teichberg fails to directly identify that the composition is in transdermal form.

Dykstra teaches that "[f]or transdermal administration, the active ingredients may be conveniently incorporated into a lipophilic carrier and formulated as a topical crème or adhesive patch" (see entire document, for instance, [0024]). It is further noted that Dykstra teaches pyruvate derivatives as preferred actives (see entire document, for instance, [0009]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the composition of Teichberg as a transdermal patch. One would have been motivated to do so since transdermal delivery is a well known method of drug delivery. There would have been a reasonable expectation of success since Teichberg teaches that the composition can comprise lipophilic vehicles, wherein Dykstra teaches that transdermal patches and topical creams are made by the composition being in a lipophilic carrier.

Conclusion

No claims allowed. All claims rejected. No claims objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR M. LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/David J Blanchard/
Primary Examiner, Art Unit 1643